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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,599	12/15/2000	Lisa K. Nolan	255.0001 0122	1240

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EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT PAPER NUMBER

1645

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/738,599	NOLAN ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 June 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30-33, 37-42, 44, 45 and 67-70 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 30-33, 69 and 70 ~~is/are~~ are allowed.
- 6) ☒ Claim(s) 37-42, 67 and 68 ~~is/are~~ are rejected.
- 7) ☒ Claim(s) 44 and 45 ~~is/are~~ are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **RESPONSE TO APPLICANTS' AMENDMENT**

### **Applicants' Amendment**

- 1) Acknowledgment is made of Applicants' amendment filed 06/08/06 in response to the non-final Office Action mailed 01/13/06.

### **Status of Claims**

- 2) Claims 35, 36, 46-66 and 71-73 have been canceled via the amendment filed 06/08/06. Claims 30-33, 37-42, 44, 45 and 67-70 are pending and are under examination.

### **Prior Citation of Title 35 Sections**

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

### **Prior Citation of References**

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

### **Rejection(s) Moot**

- 5) The rejection of claims 71-73 made in paragraph 16 of the Office Action mailed 08/10/05 and maintained in paragraph 10 of the Office Action mailed 06/08/06 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claims.
- 6) The rejection of claims 71 and 73 made in paragraph 17(a) of the Office Action mailed 08/10/05 and maintained in paragraph 11 of the Office Action mailed 06/08/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.
- 7) The rejection of claim 73 made in paragraph 17(b) of the Office Action mailed 08/10/05 and maintained in paragraph 12 of the Office Action mailed 06/08/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.
- 8) The rejection of claim 71 made in paragraph 13 of the Office Action mailed 06/08/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

### Rejection(s) Maintained

9) The rejection of claims 37-40 and 67 made in paragraph 14 of the Office Action mailed 06/08/06 under 35 U.S.C § 102(b) as being anticipated by Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess, 1990) as evidenced by Harlow *et al.* (*In: Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record) and Hunter (US 5,554,372), is maintained for reasons set forth therein and herebelow.

Applicants cite of the various Office Actions wherein the reference of Barondes *et al.* was applied as prior art. Applicants contend that the rejection lacks an essential element required to establish a *prima facie* rejection. Applicants cite MPEP 2112 and state that in relying upon the theory of inherency, the Office must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Applicants allege that the Office has not made that showing, and that the doctrine of inherency is not available to supplement the demonstrated deficiencies of Barondes *et al.* Applicants assert that Barondes *et al.* fails to teach each and every element of independent claim 37. Applicants reproduce claim 37 and contend that Barondes *et al.* does not disclose the claimed composition comprising a pharmaceutically acceptable carrier.

With regard to the teachings of Hunter, Applicants cite Hunter's sentence that the toxicity of lipopolysaccharide materials 'has impeded their development as adjuvant', and assert that the toxicity of lipopolysaccharide is well known as referenced by the text of Hunter. Applicants cite MPEP 2111.01(I) and state that there is a clear definition in the specification at lines 14-16 of page 44 of a pharmaceutically acceptable carrier as a carrier that is 'acceptable' in the sense of being compatible with the other ingredients of a composition and not deleterious to the recipient thereof. Applicants submit that since lipopolysaccharide is toxic, it would be deleterious to the recipient thereof, and therefore it cannot be considered a pharmaceutically acceptable carrier.

Applicants' arguments have been carefully considered, but are not persuasive. Applicants are correct in that the reference of Barondes *et al.* was applied more than once as prior art, with or without the as-evidenced-by reference of Harlow *et al.* and/or Hunter. In compliance with MPEP 2112, the Office did provide a factual basis and/or technical reasoning to reasonably support the determination that the intrinsic adjuvant characteristic necessarily flows from the teachings of the applied prior art reference of Barondes *et al.* Contrary to Applicants' assertion, Barondes *et al.* teach each and every element of independent claim 37. See paragraph 14 of the Office Action

mailed 06/08/06. The Office has clearly established a *prima facie* case of anticipation.

In addition to the disclosure of Hunter, the *prima facie* evidence for the fact that lipopolysaccharide serves intrinsically as an adjuvant, non-deleterious to the recipient, comes from the following prior art references.

(A) Despite the alleged toxicity, *E. coli* bacterial cells comprising LPS, or their purified LPS have been routinely administered to mammals for immunization purposes. For example, see first full paragraph in right column on page 250 of Moore *et al.* (*Transplantation* 44: 249-253, 1987).

(B) Despite the alleged deleterious effect, *E. coli* bacterial cells comprising LPS have been routinely used for immunization of humans to induce bactericidal antibodies in said humans. See the abstract of Dale *et al.* (*J. Infect. Dis.* 166: 316-325, 1992).

(C) Despite the alleged toxicity and alleged deleterious effect, immunogenic compositions comprising normal saline and live *E. coli* bacterial cells comprising LPS therein have been injected intravenously to rabbits in order to raise antisera. See section [0044] on page 6 of US 2004/0156829 A1.

The references of Moore *et al.*, Dale *et al.*, and US 2004/0156829 A1 are cited herein solely to document the art-known fact that *E. coli* cells have been injected or administered to mammals, including humans, to elicit prophylactic/therapeutic effects despite the presence of lipopolysaccharide therein. Therefore, Applicants' argument that LPS with its intrinsic adjuvant property 'is deleterious to the recipient' is simply not convincing. The rejection stands.

**10)** The rejection of claim 41 made in paragraph 15 of the Office Action mailed 06/08/06 under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) as applied to claim 37 above and further in view of Applicants' admitted state of the prior art, is maintained for reasons set forth therein and herebelow.

Applicants contend that the Office has not met the burden of establishing a *prima facie* case of obviousness. Applicants state that the rejection is identical, word by word, with the rejection present at pages 7-8, paragraph 20 of the Office Action dated 08/10/05, which was withdrawn at page 3 of paragraph 8 of the Office Action 01/13/06.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth at paragraph 15 of the Office Action mailed 06/08/06 and as further explained at paragraph 9

with regard to the teachings of Barondess *et al.* as modified by Applicants' admitted state of the prior art, the Office has clearly established a *prima facie* case of obviousness. Contrary to Applicants' assertion, the rejection of claim 41 set forth via paragraph 20 of the Office Action dated 08/10/05 and the rejection set forth via paragraph 15 of the Office Action mailed 06/08/06 are not 'identical'. The rejection of dependent claim 41 presented at paragraph 20 of the Office Action dated 08/10/05 was over Barondess *et al.* (*Nature* 344: 871-874, 1990) as applied to claim 37 'above', and further in view of Applicants' admitted state of the prior art. The base claim 37 'above' was rejected via paragraph 19 of the Office Action dated 08/10/05 under 35 U.S.C § 103 as being **unpatentable** over Barondess *et al.* (*Nature* 344: 871-874, 1990) in view of Harlow *et al.* (*In: Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988). What was withdrawn via paragraph 8 of the Office Action 01/13/06 was a 35 U.S.C § 103 obviousness rejection of claim 41.

On the other hand, the rejection of claim 41 presented at paragraph 15 of the Office Action mailed 06/08/06 is over Barondess *et al.* (*Nature* 344: 871-874, 1990) as applied to claim 37 'above', and further in view of Applicants' admitted state of the prior art. The base claim 37 'above' is rejected via paragraph 14 of the Office Action dated 06/08/06 under 35 U.S.C § 102 as being **anticipated** by Barondess *et al.* (*Nature* 344: 871-874, 1990) (Barondess *et al.*, 1990) as evidenced by Harlow *et al.* (*In: Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988) and Hunter (US 5,554,372). Therefore, Applicants' assertion that the previous rejection of claim 41 and the currently pending rejection of claim 41 are 'identical' is inaccurate. The rejection stands.

**11)** The rejection of claims 42 and 68 made in paragraph 16 of the Office Action mailed 06/08/06 under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) as applied to claim 38 above and further in view of Krieg *et al.* (WO 96/02555, already of record), is maintained for reasons set forth therein and herebelow.

Applicants contend that the Office has not met the burden of establishing a *prima facie* case of obviousness. Applicants state that the rejection of claim 42 is identical, word by word, with the rejection present at pages 8-9, paragraph 21 of the Office Action dated 08/10/05, which was withdrawn at page 3 of paragraph 9 of the Office Action 01/13/06. With regard to the rejection of claim 68, Applicants ask the Office to refer to their earlier argument submitted

11/10/05 at page 14, last paragraph through page 15. Applicants contend that although this earlier argument relates to claim 42, both claims 42 and 68 recite 'an immunostimulatory sequence'.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth at paragraph 16 of the Office Action mailed 06/08/06 and further explained at paragraph 9 regard to the teachings of Barondess *et al.* as modified by Krieg *et al.*, the Office has clearly established a *prima facie* case of obviousness. Contrary to Applicants' assertion, the rejection of claim 42 set forth via paragraph 21 of the Office Action dated 08/10/05 and the rejection set forth via paragraph 16 of the Office Action mailed 06/08/06 are not 'identical'. The rejection of dependent claim 42 presented at paragraph 21 of the Office Action dated 08/10/05 was over Barondess *et al.* (*Nature* 344: 871-874, 1990) as applied to claim 38 'above', and further in view of Krieg *et al.* (WO 96/02555). Claim 38 'above' was rejected via paragraph 19 of the Office Action dated 08/10/05 under 35 U.S.C § 103 as being **unpatentable** over Barondess *et al.* (*Nature* 344: 871-874, 1990) in view of Harlow *et al.* (*In: Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988). What was withdrawn via paragraph 9 of the Office Action mailed 01/13/06 was a 35 U.S.C § 103 obviousness rejection of claim 42.

On the other hand, the rejection of claim 42 presented at paragraph 16 of the Office Action mailed 06/08/06 is over Barondess *et al.* (*Nature* 344: 871-874, 1990) as applied to claim 38 'above', and further in view of Krieg *et al.* (WO 96/02555). Claim 38 'above' is rejected via paragraph 14 of the Office Action mailed 06/08/06 under 35 U.S.C § 102 as being **anticipated** by Barondess *et al.* (*Nature* 344: 871-874, 1990) as evidenced by Harlow *et al.* (*In: Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988) and Hunter (US 5,554,372). Therefore, Applicants' assertion that the previous rejection of claim 42 and the currently pending rejection of claim 42 are 'identical' is inaccurate. The rejection stands.

With regard to Applicants' remarks on the Office's rejection of claim 68, it should be noted that claims 68 and 42 are not identical in scope and in words. Applicants' earlier arguments related to the rejection of claim 42 as submitted on pages 14 and 15 of Applicants' amendment filed 11/10/05 are *not* pertinent to the currently pending rejection of claim 68 for similar reasons explained above.

### Remarks

12) Claims 37-42, 67 and 68 stand rejected. Claims 30-33, 69 and 70 are allowed. Claims 44 and 45 are objected to for being dependent from a rejected claim.

**13) THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

**14)** Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Central Fax number (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

**15)** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.Mov>. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**16)** Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

  
S. DEVI, PH.D.  
PRIMARY EXAMINER